MMP-13 inhibitors

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEXO1623

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 21	IPC search and display fields enhanced in CA/CAplus with the IPC reform
NEWS 4	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 5	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 6	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 7	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 8	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 9	JAN 30	Saved answer limit increased
NEWS 10	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS 11	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 12	FEB 22	Status of current WO (PCT) information on STN
NEWS 13	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 14	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 15	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 16	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 17	FEB 28	TOXCENTER reloaded with enhancements
NEWS 18	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 19	MAR 01	INSPEC reloaded and enhanced
NEWS 20	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 21	MAR 08	X.25 communication option no longer available after June 2006
NEWS 22	MAR 22	EMBASE is now updated on a daily basis
NEWS 23	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 24	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT http://download.cas.org/express/v8.0-Discover/

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation

MMP-13 inhibitors

of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:29:34 ON 03 APR 2006

=> file medline biosis
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 13:29:57 ON 03 APR 2006

FILE 'BIOSIS' ENTERED AT 13:29:57 ON 03 APR 2006
Copyright (c) 2006 The Thomson Corporation

=> s TIMP
L1 9810 TIMP

=> s matrix(w)metalloprotease(w)13
L2 38 MATRIX(W) METALLOPROTEASE(W) 13

=> s MMP-13
L3 1547 MMP-13

=> s L1 and (L2 or L3)
L4 374 L1 AND (L2 OR L3)

=> s L4 and allosteric
L5 0 L4 AND ALLOSTERIC

=> s L4 and noncompetitive
L6 0 L4 AND NONCOMPETITIVE

=> s L4 and binding
L7 23 L4 AND BINDING

=> s L4 and structure
L8 8 L4 AND STRUCTURE

=> d L8 1-8 ti

L8 ANSWER 1 OF 8 MEDLINE on STN
TI Cellular activation of proMMP-13 by MT1-MMP depends on the C-terminal domain of **MMP-13.**

L8 ANSWER 2 OF 8 MEDLINE on STN
TI Biochemical characterization of human collagenase-3.

L8 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Differential expression of matrix metalloproteinases in vernal keratoconjunctivitis, allergic asthma and nasal polyps.

L8 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Plasma profiles of matrix metalloproteinases and tissue inhibitors of matrix metalloproteinases: Changes associated with the presence of diastolic dysfunction.

L8 ANSWER 5 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Temporal plasma profiles of matrix metalloproteinases and tissue inhibitors of matrix metalloproteinases in patients with left ventricular hypertrophy.

MMP-13 inhibitors

L8 ANSWER 6 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Expression profile of trophoblast invasion-associated genes in the pre-eclamptic placenta.

L8 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Matrix metalloproteinases and atrial structural remodeling.

L8 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Matrix metalloproteinases and their inhibitors in gestational trophoblastic diseases and normal placenta.

=> d 2 ti abs bib

L8 ANSWER 2 OF 8 MEDLINE on STN
TI Biochemical characterization of human collagenase-3.
AB The cDNA of a novel matrix metalloproteinase, collagenase-3 (**MMP-13**) has been isolated from a breast tumor library (Freije, J. M. P., Dicz-Itza, I., Balbin, M., Sanchez, L. M., Blasco, R., Tolivia, J., and Lopez-Otin, C. (1994) J. Biol. Chemical 269, 16766-16773), and a potential role in tumor progression has been proposed for this enzyme. In order to establish the possible role of collagenase-3 in connective tissue turnover, we have expressed and purified recombinant human procollagenase-3 and characterized the enzyme biochemically. The purified procollagenase-3 was shown to be glycosylated and displayed a M(r) of 60,000, the N-terminal sequence being LPLPSGGD, which is consistent with the cDNA-predicted sequence. The proenzyme was activated by p-aminophenylmercuric acetate or stromelysin, yielding an intermediate form of M(r) 50,000, which displayed the N-terminal sequence L58EVTGK. Further processing resulted in cleavage of the Glu84-Tyr85 peptide bond to the final active enzyme (M(r) 48,000). Trypsin activation of procollagenase-3 also generated a Tyr85 N terminus, but it was evident that the C-terminal domain was rapidly lost, and hence the collagenolytic activity diminished. Analysis of the substrate specificity of collagenase-3 revealed that soluble type II collagen was preferentially hydrolyzed, while the enzyme was 5 or 6 times less efficient at cleaving type I or III collagen. Fibrillar type I collagen was cleaved with comparable efficiency to the fibroblast and neutrophil collagenases (MMP-1 and MMP-8), respectively. Unlike these collagenases, gelatin and the peptide substrates Mea-Pro-Leu-Gly-Leu-Dpa-Ala-Arg-NH2 and Mca-Pro-Cha-Gly-Nva-His-Ala-Dpa-NH2 were efficiently hydrolyzed as well, as would be predicted from the similarities between the active site sequence of collagenase-3 (**MMP-13**) and the gelatinases A and B. Active collagenase-3 was inhibited in a 1:1 stoichiometric fashion by the tissue inhibitors of metalloproteinases, **TIMP**-1, **TIMP**-2, and **TIMP**-3. These results suggest that in vivo collagenase-3 could play a significant role in the turnover of connective tissue matrix constituents.
AN 96139488 MEDLINE
DN PubMed ID: 8576151
TI Biochemical characterization of human collagenase-3.
AU Knauper V; Lopez-Otin C; Smith B; Knight G; Murphy G
CS Strangeways Research Laboratory, Department of Cell and Molecular Biology, Worts' Causeway, Cambridge, United Kingdom.
SO The Journal of biological chemistry, (1996 Jan 19) Vol. 271, No. 3, pp. 1544-50.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199603

MMP-13 inhibitors

ED Entered STN: 19960321
Last Updated on STN: 19970203
Entered Medline: 19960311

=> d L7 1-23 ti

L7 ANSWER 1 OF 23 MEDLINE on STN
TI Localization of matrix metalloproteinases, (MMPs) their tissue inhibitors, and vascular endothelial growth factor (VEGF) in growth plates of children and adolescents indicates a role for MMPs in human postnatal growth and skeletal maturation.

L7 ANSWER 2 OF 23 MEDLINE on STN
TI Mechanical overload induces VEGF in cartilage discs via hypoxia-inducible factor.

L7 ANSWER 3 OF 23 MEDLINE on STN
TI Cyclic tensile strain and cyclic hydrostatic pressure differentially regulate expression of hypertrophic markers in primary chondrocytes.

L7 ANSWER 4 OF 23 MEDLINE on STN
TI Expression profiles of collagens, HSP47, TGF-beta1, MMPs and TIMPs in epidermolysis bullosa acquisita.

L7 ANSWER 5 OF 23 MEDLINE on STN
TI Release of matrix metalloproteinases following alcohol septal ablation in hypertrophic obstructive cardiomyopathy.

L7 ANSWER 6 OF 23 MEDLINE on STN
TI Macrophage migration inhibitory factor up-regulates matrix metalloproteinase-9 and -13 in rat osteoblasts. Relevance to intracellular signaling pathways.

L7 ANSWER 7 OF 23 MEDLINE on STN
TI Cyclosporin A inhibition of aggrecanase-mediated proteoglycan catabolism in articular cartilage.

L7 ANSWER 8 OF 23 MEDLINE on STN
TI Relaxin inhibits effective collagen deposition by cultured hepatic stellate cells and decreases rat liver fibrosis in vivo.

L7 ANSWER 9 OF 23 MEDLINE on STN
TI Oncostatin M-induced matrix metalloproteinase and tissue inhibitor of metalloproteinase-3 genes expression in chondrocytes requires Janus kinase/STAT signaling pathway.

L7 ANSWER 10 OF 23 MEDLINE on STN
TI Overexpression of epidermal growth factor receptor in human head and neck squamous carcinoma cell lines correlates with matrix metalloproteinase-9 expression and in vitro invasion.

L7 ANSWER 11 OF 23 MEDLINE on STN
TI Interleukin-6 increases rat metalloproteinase-13 gene expression through stimulation of activator protein 1 transcription factor in cultured fibroblasts.

L7 ANSWER 12 OF 23 MEDLINE on STN
TI The role of the C-terminal domain of human collagenase-3 (**MMP-13**) in the activation of procollagenase-3, substrate specificity, and tissue inhibitor of metalloproteinase interaction.

L7 ANSWER 13 OF 23 MEDLINE on STN

MMP-13 inhibitors

TI Biochemical characterization of human collagenase-3.

L7 ANSWER 14 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Chondrocyte calcium-sensing receptor and PTHrP are up-regulated in osteoarthritis and promote matrix catabolism.

L7 ANSWER 15 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Cell density-dependent regulation of matrix metalloproteinase and **TIMP** expression in differently tumorigenic breast cancer cell lines.

L7 ANSWER 16 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Expression profiles of collagens, HSP47, TGF-beta1, MMPs and TIMPs in epidermolysis bullosa acquisita.

L7 ANSWER 17 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Release of matrix metalloproteinases following alcohol septal ablation in hypertrophic obstructive cardiomyopathy.

L7 ANSWER 18 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Relaxin inhibits effective collagen deposition by cultured hepatic stellate cells and decreases rat liver fibrosis in vivo.

L7 ANSWER 19 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Interleukin-6 increases rat metalloproteinase-13 gene expression through stimulation of activator protein 1 transcription factor in cultured fibroblasts.

L7 ANSWER 20 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Molecular interactions between the plasminogen/plasmin and matrix metalloproteinase systems.

L7 ANSWER 21 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Studies suggesting new potential roles for pancreatic stone protein in inflammatory bowel disease: Identification of extracellular matrix **binding** and interactions with matrix metalloproteinases.

L7 ANSWER 22 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Overexpression of epidermal growth factor receptor in human head and neck squamous carcinoma cell lines correlates with matrix metalloproteinase-9 expression and in vitro invasion.

L7 ANSWER 23 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI The role of the C-terminal domain of human collagenase-3 (**MMP-13**) in the activation of procollagenase-3, substrate specificity, and tissue inhibitor of metalloproteinase interaction.

=> s L4 and mechanism
L9 15 L4 AND MECHANISM

=> s TIMP and allosteric
L10 0 TIMP AND ALLOSTERIC

MMP-13 inhibitors

=> s metalloprotease and allosteric
L11 5 METALLOPROTEASE AND ALLOSTERIC

=> d 1-5 ti

L11 ANSWER 1 OF 5 MEDLINE on STN
TI Recent advances in the design of matrix **metalloprotease** inhibitors.

L11 ANSWER 2 OF 5 MEDLINE on STN
TI The role of the N-terminal propeptide of the pro-aminopeptidase processing protease: refolding, processing, and enzyme inhibition.

L11 ANSWER 3 OF 5 MEDLINE on STN
TI Arg(1098) is critical for the chloride dependence of human angiotensin I-converting enzyme C-domain catalytic activity.

L11 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Enzymatic characterization of the streptococcal endopeptidase, IdeS, reveals that it is a cysteine protease with strict specificity for IgG cleavage due to exosite binding.

L11 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI The role of the N-terminal propeptide of the pro-aminopeptidase processing protease: Refolding, processing, and enzyme inhibition.

=> d 1 ti abs bib

L11 ANSWER 1 OF 5 MEDLINE on STN
TI Recent advances in the design of matrix **metalloprotease** inhibitors.
AB Inhibition of matrix metalloproteases (MMPs) for the treatment of diseases, such as cancer, arthritis and other diseases associated with tissue remodeling, has become an area of intense interest in the pharmaceutical industry in recent years. Despite tremendous efforts over the last decade to explore individual members of this target family, along with multiple inhibitor classes, simple and effective drugs for inhibiting individual MMPs have not yet emerged. This review highlights the major developments in research into MMPs and their inhibitors, from the recent medicinal chemistry literature, with a focus on structure-based design, selectivity and pharmacokinetic (PK) properties. The increasing availability of high-resolution X-ray crystal structures for many members of this protein family makes MMPs ideally suited for structure-based design approaches, which are now routinely used in this area. The most challenging aspect of lead optimization for MMP inhibitors is in finding candidates having acceptable pharmacological, PK and selectivity profiles. Clinical trials in cancer giving disappointing results have led to discussions on how to gain adequate MMP selectivity in order to minimize side effects. Unfortunately, careful analysis of X-ray crystal structures has not suggested any simple solutions. These areas collectively constitute the main challenges in the current search for orally available MMP inhibitors, and will be discussed in this review.
AN 2004433518 MEDLINE
DN PubMed ID: 15338961
TI Recent advances in the design of matrix **metalloprotease** inhibitors.
AU Matter Hans; Schudok Manfred
CS Aventis Pharma Deutschland GmbH, DI&A Chemistry, Building G 878, D-65926, Frankfurt am Main, Germany.. hans.matter@aventis.com
SO Current opinion in drug discovery & development, (2004 Jul) Vol. 7, No. 4, pp. 513-35. Ref: 133

MMP-13 inhibitors

Journal code: 100887519. ISSN: 1367-6733.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200409
ED Entered STN: 20040902
Last Updated on STN: 20040929
Entered Medline: 20040928

=> d l9 1-15 ti

L9 ANSWER 1 OF 15 MEDLINE on STN
TI Increased expression of matrix metalloproteinase-2, matrix metalloproteinase-9 and matrix metalloproteinase-13 in lesional skin of bullous pemphigoid.

L9 ANSWER 2 OF 15 MEDLINE on STN
TI The induction of matrix metalloproteinase and cytokine expression in synovial fibroblasts stimulated with immune cell microparticles.

L9 ANSWER 3 OF 15 MEDLINE on STN
TI Matrix metalloproteinase expression is related to angiogenesis and histologic grade in spindle cell soft tissue neoplasms of the extremities.

L9 ANSWER 4 OF 15 MEDLINE on STN
TI Insulin-like growth factor 1 blocks collagen release and down regulates matrix metalloproteinase-1, -3, -8, and -13 mRNA expression in bovine nasal cartilage stimulated with oncostatin M in combination with interleukin 1alpha.

L9 ANSWER 5 OF 15 MEDLINE on STN
TI Stromelysin (MMP-3) synthesis is up-regulated in estrogen-deficient mouse osteoblasts in vivo and in vitro.

L9 ANSWER 6 OF 15 MEDLINE on STN
TI The role of the C-terminal domain of human collagenase-3 (**MMP-13**) in the activation of procollagenase-3, substrate specificity, and tissue inhibitor of metalloproteinase interaction.

L9 ANSWER 7 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Systemic regulation of angiogenesis and matrix degradation in bone regeneration - Distraction osteogenesis compared to rigid fracture healing.

L9 ANSWER 8 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Cell density-dependent regulation of matrix metalloproteinase and **TIMP** expression in differently tumorigenic breast cancer cell lines.

L9 ANSWER 9 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI The induction of matrix metalloproteinase and cytokine expression in synovial fibroblasts stimulated with immune cell microparticles.

L9 ANSWER 10 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Matrix metalloproteinase expression is related to angiogenesis and histologic grade in spindle cell soft tissue neoplasms of the extremities.

L9 ANSWER 11 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

MMP-13 inhibitors

TI Suppressive effect of leflunomide metabolite (A77 1726) on metalloproteinase production in IL-1beta stimulated rheumatoid synovial fibroblasts.

L9 ANSWER 12 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Influence of matrine on the preliferation and collagen synthesis of cultured neonatal rat cardic fibroblast stimulated by angiotensin II.

L9 ANSWER 13 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Insulin-like growth factor 1 blocks collagen release and down regulates matrix metalloproteinase-1, -3, -8, and -13 mRNA expression in bovine nasal cartilage stimulated with oncostatin M in combination with interleukin 1alpha.

L9 ANSWER 14 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Stromelysin (MMP-3) synthesis is up-regulated in estrogen-deficient mouse osteoblasts in vivo and in vitro.

L9 ANSWER 15 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI The role of the C-terminal domain of human collagenase-3 (**MMP-13**) in the activation of procollagenase-3, substrate specificity, and tissue inhibitor of metalloproteinase interaction.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	5.87	6.08

FILE 'STNGUIDE' ENTERED AT 13:35:32 ON 03 APR 2006
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Mar 31, 2006 (20060331/UP).

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	6.14

STN INTERNATIONAL LOGOFF AT 13:36:08 ON 03 APR 2006

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptaexo1623

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

MMP-13 inhibitors

```
* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  DEC 21   IPC search and display fields enhanced in CA/CAplus with the
                   IPC reform
 NEWS  4  DEC 23   New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
                   USPAT2
 NEWS  5  JAN 13   IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
 NEWS  6  JAN 13   New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
                   INPADOC
 NEWS  7  JAN 17   Pre-1988 INPI data added to MARPAT
 NEWS  8  JAN 17   IPC 8 in the WPI family of databases including WPIFV
 NEWS  9  JAN 30   Saved answer limit increased
 NEWS 10  JAN 31   Monthly current-awareness alert (SDI) frequency
                   added to TULSA
 NEWS 11  FEB 21   STN AnaVist, Version 1.1, lets you share your STN AnaVist
                   visualization results
 NEWS 12  FEB 22   Status of current WO (PCT) information on STN
 NEWS 13  FEB 22   The IPC thesaurus added to additional patent databases on STN
 NEWS 14  FEB 22   Updates in EPFULL; IPC 8 enhancements added
 NEWS 15  FEB 27   New STN AnaVist pricing effective March 1, 2006
 NEWS 16  FEB 28   MEDLINE/LMEDLINE reload improves functionality
 NEWS 17  FEB 28   TOXCENTER reloaded with enhancements
 NEWS 18  FEB 28   REGISTRY/ZREGISTRY enhanced with more experimental spectral
                   property data
 NEWS 19  MAR 01   INSPEC reloaded and enhanced
 NEWS 20  MAR 03   Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS 21  MAR 08   X.25 communication option no longer available after June 2006
 NEWS 22  MAR 22   EMBASE is now updated on a daily basis
 NEWS 23  APR 03   New IPC 8 fields and IPC thesaurus added to PATDPAFULL
 NEWS 24  APR 03   Bibliographic data updates resume; new IPC 8 fields and IPC
                   thesaurus added in PCTFULL

 NEWS EXPRESS  FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
               V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
               http://download.cas.org/express/v8.0-Discover/

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:48:56 ON 03 APR 2006

=> file medline biosis caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21
```

MMP-13 inhibitors

FILE 'MEDLINE' ENTERED AT 13:49:35 ON 03 APR 2006

FILE 'BIOSIS' ENTERED AT 13:49:35 ON 03 APR 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 13:49:35 ON 03 APR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

=> s metalloprotease and (allosteric or noncompetitive)
L1 20 METALLOPROTEASE AND (ALLOSTERIC OR NONCOMPETITIVE)

=> s ((metalloprotease(w)13) or MMP-13) and (allosteric or noncompetitive)
L2 11 ((METALLOPROTEASE(W) 13) OR MMP-13) AND (ALLOSTERIC OR NONCOMPET
ITIVE)

=> d L2 1-11 ti

L2 ANSWER 1 OF 11 MEDLINE on STN
TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline: relationship to structure of the enzyme.

L2 ANSWER 2 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline: Relationship to structure of the enzyme.

L2 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Combination of an **allosteric** inhibitor of matrix metalloproteinase-13 and a ligand to an alpha-2-delta receptor

L2 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Combination of an **allosteric** alkyne inhibitor of matrix metalloproteinase-13 with a selective inhibitor of cyclooxygenase-2

L2 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Combination of an **allosteric** inhibitor of matrix metalloproteinase-13 with a selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib

L2 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Combination of an **allosteric** carboxylic inhibitor of matrix metalloproteinase-13 with a selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use

L2 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Combination of an **allosteric** alkyne inhibitor of matrix metalloproteinase-13 with celecoxib or valdecoxib, pharmaceutical compositions, and therapeutic use

L2 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Combination of an **allosteric** inhibitor of matrix metalloproteinase-13 with celecoxib or valdecoxib, pharmaceutical compositions, and therapeutic use

L2 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Combination of an **allosteric** carboxylic inhibitor of matrix metalloproteinase-13 with celecoxib or valdecoxib, pharmaceutical compositions, and therapeutic use

L2 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Rapid identification and classification of metalloenzyme inhibitors using ligands to the functional metal cation

MMP-13 inhibitors

L2 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline. relationship to structure of the enzyme

=> s L2 and py<2003
1 FILES SEARCHED...
L3 3 L2 AND PY<2003

=> d L3 1-3 ti

L3 ANSWER 1 OF 3 MEDLINE on STN
TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline: relationship to structure of the enzyme.

L3 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline: Relationship to structure of the enzyme.

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline. relationship to structure of the enzyme

=> d 1-3 ti abs bib

L3 ANSWER 1 OF 3 MEDLINE on STN
TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline: relationship to structure of the enzyme.
AB OBJECTIVE: To investigate the inhibition of matrix metalloproteinase 1 (MMP-1), MMP-8, and **MMP-13** by doxycycline, and to determine whether the variable hemopexin-like domain of each MMP was responsible for the differences in susceptibility to doxycycline inhibition among these collagenases. METHODS: Recombinant human MMP-1 (collagenase 1), MMP-8 (collagenase 2), and **MMP-13** (collagenase 3), truncated forms of MMP-8 and **MMP-13** lacking the hemopexin-like domain, and a mutant form of truncated **MMP-13** were used in these studies. The activity of the full-length MMP in the presence of doxycycline was tested against type II collagen, a natural substrate for the enzymes. A small peptolide substrate was used to determine which structural features of the MMPs were related to sensitivity to doxycycline inhibition. RESULTS: The activity of **MMP-13** and MMP-8 against type II collagen was inhibited by 50-60% by 30 microM doxycycline, while that of MMP-1 was inhibited only 18% by 50 microM doxycycline. In contrast, in experiments with the peptolide substrate, neither full-length nor truncated **MMP-13** was inhibited until the concentration of the drug exceeded 90 microM. MMP-8 and truncated MMP-8 were sensitive to inhibition by 30 microM doxycycline, while MMP-1 was slightly inhibited (14%) by 90 microM doxycycline. For MMP-8, inhibition was reversible upon dilution and was independent of the order in which the reagents were added. Kinetic analysis of the inhibition constant (K(i)) of MMP-8 (K(i) = 36 microM) and truncated MMP-8 (K(i) = 77 microM) indicated that inhibition was **noncompetitive.** CONCLUSION: Significant inhibition of **MMP-13** and MMP-8 activity against collagen occurred in vitro at concentrations that were near the concentrations achieved in serum after oral dosing. Studies with truncated enzymes and 2 substrates suggest that doxycycline disrupts the conformation of the hemopexin-like domain of **MMP-13** and the catalytic domain of MMP-8.
AN 1999292228 MEDLINE
DN PubMed ID: 10366106

MMP-13 inhibitors

TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline: relationship to structure of the enzyme.
AU Smith G N Jr; Mickler E A; Hasty K A; Brandt K D
CS Rheumatology Division, Indiana University School of Medicine, Indianapolis 46202-5103, USA.
NC AR-20582 (NIAMS)
AR-39166 (NIAMS)
SO Arthritis and rheumatism, **(1999 Jun)** Vol. 42, No. 6, pp. 1140-6.
Journal code: 0370605. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199906
ED Entered STN: 19990714
Last Updated on STN: 20000303
Entered Medline: 19990625

L3 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline: Relationship to structure of the enzyme.
AB Objective. To investigate the inhibition of matrix metalloproteinase 1 (MMP-1), MMP-8, and **MMP-13** by doxycycline, and to determine whether the variable hemopexin-like domain of each MMP was responsible for the differences in susceptibility to doxycycline inhibition among these collagenases. Methods. Recombinant human MMP-1 (collagenase 1), MMP-8 (collagenase 2), and **MMP-13** (collagenase 3), truncated forms of MMP-8 and **MMP-13** lacking the hemopexin-like domain, and a mutant form of truncated **MMP-13** were used in these studies. The activity of the full-length MMP in the presence of doxycycline was tested against type II collagen, a natural substrate for the enzymes. A small peptolide substrate was used to determine which structural features of the MMPs were related to sensitivity to doxycycline inhibition. Results. The activity of **MMP-13** and MMP-8 against type II collagen was inhibited by 50-60% by 30 muM doxycycline, while that of MMP-1 was inhibited only 18% by 50 muM doxycycline. Incontrast, in experiments with the peptolide substrate, neither full-length nor truncated **MMP-13** was inhibited until the concentration of the drug exceeded 90 muM. MMP-8 and truncated MMP-8 were sensitive to inhibition by 30 muM doxycycline, while MMP-1 was slightly inhibited (14%) by 90 muM doxycycline. For MMP-8, inhibition was reversible upon dilution and was independent of the order in which the reagents were added. Kinetic analysis of the inhibition constant (Ki) of MMP-8 (Ki = 36 muM) and truncated MMP-8 (Ki = 77 muM) indicated that inhibition was **noncompetitive.** Conclusion. Significant inhibition of **MMP-13** and MMP-8 activity against collagen occurred in vitro at concentrations that were near the concentrations achieved in serum after oral dosing. Studies with truncated enzymes and 2 substrates suggest that doxycycline disrupts the conformation of the hemopexin-like domain of **MMP-13** and the catalytic domain of MMP-8.
AN 1999:324142 BIOSIS
DN PREV199900324142
TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline: Relationship to structure of the enzyme.
AU Smith, Gerald N., Jr. [Reprint author]; Mickler, Elizabeth A.; Hasty, Karen A.; Brandt, Kenneth D.
CS Rheumatology Division, Indiana University School of Medicine, 541 Clinical Drive, Room 492, Indianapolis, IN, 46202-5103, USA
SO Arthritis and Rheumatism, (**June, 1999**) Vol. 42, No. 6, pp. 1140-1146. print.
CODEN: ARHEAW. ISSN: 0004-3591.
DT Article

MMP-13 inhibitors

LA English
ED Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline. relationship to structure of the enzyme
AB Objectives: to investigate the inhibition of matrix metalloproteinase 1 (MMP-1), MMP-8, and **MMP-13** by doxycycline, and to determine whether the variable hemopexin-like domain of each MMP was responsible for the differences in susceptibility to doxycycline inhibition among these collagenases. Recombinant human MMP-1 (collagenase 1), MMP-8 (collagenase 2), and **MMP-13** (collagenase 3), truncated forms of MMP-8 and **MMP-13** lacking the hemopexin-like domain, and a mutant form of truncated **MMP-13** were used in these studies. The activity of the full-length MMP in the presence of doxycycline was tested against type II collagen, a natural substrate for the enzymes. A small peptolide substrate was used to determine which structural features of the MMPs were related to sensitivity to doxycycline inhibition. The activity of **MMP-13** and MMP-8 against type II collagen was inhibited by 50-60% by 30 μM doxycycline, while that of MMP-1 was inhibited only 18% by 50 μM doxycycline. In contrast, in expts. with the peptolide substrate, neither full-length nor truncated **MMP-13** was inhibited until the concentration of the drug exceeded 90 μM. MMP-8 and truncated MMP-8 were sensitive to inhibition by 30 μM doxycycline, while MMP-1 was slightly inhibited (14%) by 90 μM doxycycline. For MMP-8, inhibition was reversible upon dilution and was independent of the order in which the reagents were added. Kinetic anal. of the inhibition constant (Ki) of MMP-8 (Ki = 36 μM) and truncated MMP-8 (Ki = 77 μM) indicated that inhibition was **noncompetitive.** Significant inhibition of **MMP-13** and MMP-8 activity against collagen occurred in vitro at concns. that were near the concns. achieved in serum after oral dosing. Studies with truncated enzymes and 2 substrates suggest that doxycycline disrupts the conformation of the hemopexin-like domain of **MMP-13** and the catalytic domain of MMP-8.
AN 1999:403357 CAPLUS
DN 131:208774
TI Specificity of inhibition of matrix metalloproteinase activity by doxycycline. relationship to structure of the enzyme
AU Smith, Gerald N., Jr.; Mickler, Elizabeth A.; Hasty, Karen A.; Brandt, Kenneth D.
CS Rheumatology Division, Indiana University School of Medicine, Indianapolis, IN, 46202-5103, USA
SO Arthritis & Rheumatism (**1999**), 42(6), 1140-1146
CODEN: ARHEAW; ISSN: 0004-3591
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:n

=> s L1 and py<2003
1 FILES SEARCHED...
L4 17 L1 AND PY<2003

=> dup rem L4
PROCESSING COMPLETED FOR L4

MMP-13 inhibitors

L5 11 DUP REM L4 (6 DUPLICATES REMOVED)

=> d l5 1-11 ti

L5 ANSWER 1 OF 11 MEDLINE on STN DUPLICATE 1
TI The role of the N-terminal propeptide of the pro-aminopeptidase processing protease: refolding, processing, and enzyme inhibition.

L5 ANSWER 2 OF 11 MEDLINE on STN
TI Arg(1098) is critical for the chloride dependence of human angiotensin I-converting enzyme C-domain catalytic activity.

L5 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Mechanism of action of clostridial neurotoxins and rational inhibitor design

L5 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Tetanus and botulinum toxins are zinc metalloproteases: molecular mechanisms and inhibition of neurotoxicity

L5 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI The **allosteric**-type mechanism of tetanus toxin **metalloprotease** activity determines its substrate specificity

L5 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Solid-phase activity assay for biologically active substances

L5 ANSWER 7 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 2
TI A kinetic comparison of the homologous proteases astacin and meprin A.

L5 ANSWER 8 OF 11 MEDLINE on STN DUPLICATE 3
TI Crystallographic structures of the elastase of Pseudomonas aeruginosa.

L5 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Effect of divalent metal ions on collagenase from Clostridium histolyticum

L5 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Kinetic evidence for cooperative binding of two orthophenanthroline molecules to Astacus protease during metal removal

L5 ANSWER 11 OF 11 MEDLINE on STN DUPLICATE 4
TI Kinetic analysis by stopped-flow radiationless energy transfer studies: effect of anions on the activity of carboxypeptidase A.

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	36.50	36.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.75	-0.75

STN INTERNATIONAL LOGOFF AT 13:54:51 ON 03 APR 2006